Recurrent Inactive Hydatid Cyst of the Liver Causing Restrictive Pulmonary Physiology

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Abstract

Hydatid and alveolar cysts are formed by the helminths Echinococcus granulosus *and* Echinococcus multilocularis*, respectively, which are endemic to pastoral areas, and are more commonly found in South America, the Mediterranean, Russia, and China. Hydatid cysts can cause bacteremia, form abscesses, or cause mass effect by compressing surrounding organs. Strategies to prevent such complications include benzimidazoles, surgical resection, and Puncture, Aspiration, Injection and Re-aspiration (PAIR) procedure. A 71-year-old Egyptian man with remote history of* Echinococcus *infection one year status post PAIR procedure, presented with dyspnea on exertion. On exam, the patient had a palpable right upper quadrant mass. The patient had a known small hydatid liver cyst on prior ultrasound, however repeat imaging showed growth to 15x19x14cm, with right hemidiaphragm elevation, compressive atelectasis, and compression of the right atrium. He had no peripheral eosinophilia and negative echinococcal serology, consistent with remote infection. The patient underwent repeat PAIR procedure and 3L of serous fluid was drained from the cyst. Fluid analysis was negative for scolices, cysts or hooklets. His symptoms improved; however the cyst re-accumulated 1 month later. Total cystectomy was performed surgically by hepatic wedge resection, with permanent improvement in symptoms. This case is a rare example of* Echinococcus *infection causing significant respiratory morbidity requiring repeated invasive procedures and surgery, in the setting of inactive disease.*

Keywords

hydatid cyst, Echinococcus granulosus*, PAIR procedure, cystic echinococcosis*

Abbreviations

ADLs = Activities of Daily Living
AE = Alveolar Echinococcosis
CE = Cystic Echinococcosis
CT = Computed Tomography
FEV_1 = Forced Expiratory Volume in 1 second
FVC = Forced Vital Capacity
IWGE = Informal Working Group on Echinococcosis
OHS = Obesity Hypoventilation Syndrome
OSA = Obstructive Sleep Apnea
PAIR = Puncture, Aspiration, Injection and Re-aspiration
RUQUS = Right Upper Quadrant Ultrasound
WHO = World Health Organization

Introduction

Hydatid cysts are formed from the larva of the helminthic organism *Echinococcus granulosus.* This helminth is endemic to pastoral areas of the Mediterranean, China, Russia, Eastern Europe, and South America. It lives its normal life cycle within its definitive hosts, and transmission to humans occurs when eggs released in feces of the host are ingested by humans via contaminated soil, water, and food.[1] Eggs, once ingested, hatch in the small bowel and penetrate the intestinal wall, migrating into various organs, where they develop into cysts. *E. granulosus* frequently forms liver cysts, causing Cystic Echinococcosis (CE), while *E. multilocularis* often forms intrapulmonary cysts, causing Alveolar Echinococcosis (AE). Cysts can be found in nearly any organ system, but hepatic hydatid cysts remain the most common by a large margin.[2,3]

Within endemic areas, annual incidence of CE ranges from <1 to 200 per 100,000 persons.[1] Prevalence varies, but is generally above 20% in such areas.[3] Most infected individuals within the United States are immigrants, believed to be infected within their country of origin; the majority are of Asian, Hispanic, or Pacific Islander descent. In endemic countries, rural areas are most affected due to the presence of sheep, goats, and canines which serve as preferred hosts.[4-6]

Symptoms of human CE may take years to manifest. In the first year of growth, cysts may expand rapidly by 5-10cm, but in subsequent years, the growth rate slows, and on average ranges from 1mm to 10mm yearly.[1] Common sequelae of CE include anaphylaxis and secondary hydatidosis (seeding of the peritoneum); if the cyst should rupture or erode into the biliary tree; intrahepatic cysts are known to cause obstructive jaundice. They can also, through virtue of their size and location, exert pressure on surrounding organs, usually resulting in chronic abdominal pain. Hydatid cysts located within the abdomen are known to cause jaundice, abdominal pain, and nausea, but are not generally known to cause pulmonary dysfunction via mass effect.[2,3]

Cysts are both diagnosed and staged via ultrasound, using the World Health Organization—Informal Working Group on Echinococcosis (WHO-IWGE) classification system (Table 1).[1,7,8] Radiographic appearance of septations, calcifications, and membranes determines the cyst activity level. Laboratory diagnosis can be confirmatory when imaging studies are not conclusive. For initial screening, ELISA is the most sensitive test, and confirmation can be performed with the echinococcal antigen immunoblot.[3,9] However, intact cysts can illicit little response from the host compared to a leaking or ruptured cyst; therefore a negative test does not rule out echinococcal disease.[1,4] Peripheral eosinophilia supports the diagnosis of active infec-

tion; however, it is not a sensitive or specific finding. Acid-fast sputum and bronchial alveolar lavage can detect hooklets and protoscolices (both indicating the presence of infectious form of the organism), however a high index of suspicion must be present to order the stains, and they are not positive in all active disease.

Treatment modality depends on the presence of serum markers indicating active infection, as well as ultrasound imaging to determine if the cyst is active, transitional, or inactive (Table 1). Cysts of stage CE4 and CE5 are observed, without active intervention.[1-3,6] For active cysts, treatment strategies utilize a combination of observation, benzimidazoles, Puncture, Aspiration, Injection and Re-aspiration (PAIR) procedure, and, in certain cases, surgical cystectomy.[1,2,10,11] We present a unique case of a large hydatid cyst in the liver causing restrictive lung disease through right hemidiaphragm elevation, treated with repeated PAIR procedures and ultimately surgical resection, despite serologically and radiographically inactive disease.

Case Presentation

A 71-year-old man of Egyptian descent presented to the pulmonology clinic with several months of progressive dyspnea on exertion and orthopnea. Medical history included paroxysmal atrial fibrillation, obstructive sleep apnea (OSA), obesity hypoventilation syndrome (OHS), and a remote history of *E. granulosus* infection for which he underwent successful PAIR procedure one year prior. The patient was initially evaluated by Cardiology to rule out atherosclerotic coronary artery disease or dysrhythmias. Coronary CT and cardiac event monitoring were not supportive of a cardiac etiology.

Prior to this presentation, the patient had a baseline home oxygen requirement of 2 liters/minute secondary to his underlying OSA/OHS. Despite no reported changes in lifestyle or oxygen use in the past year, the patient became more symptomatic, and was unable to perform activities of daily living (ADLs). He underwent further evaluation with spirometry, chest radiograph,

Table 1. Scheme of differentiation for human CE on ultrasound, as described by the World Health Organization.

STATUS	CLASS	DESCRIPTION
UNDIFFERENTIATED	CL	Unilocular anechoic cystic lesion without internal echoes/septation
ACTIVE	CE1	Uniformly anechoic cyst with fine echoes settled in it (hydatid sand)
ACTIVE	CE2	Cyst with multiple septation; multivesicular/rosette/honeycomb appearance with unilocular mother cyst
TRANSITIONAL	CE3	Unilocular cyst, with daughter cysts with detached laminated membranes (water lily sign)
INACTIVE	CE4	Mixed hypo- and hyperechoic contents, with absent daughter cysts (ball of wool sign)
INACTIVE	CE5	Arch-like, thick, partially or completely calcified wall

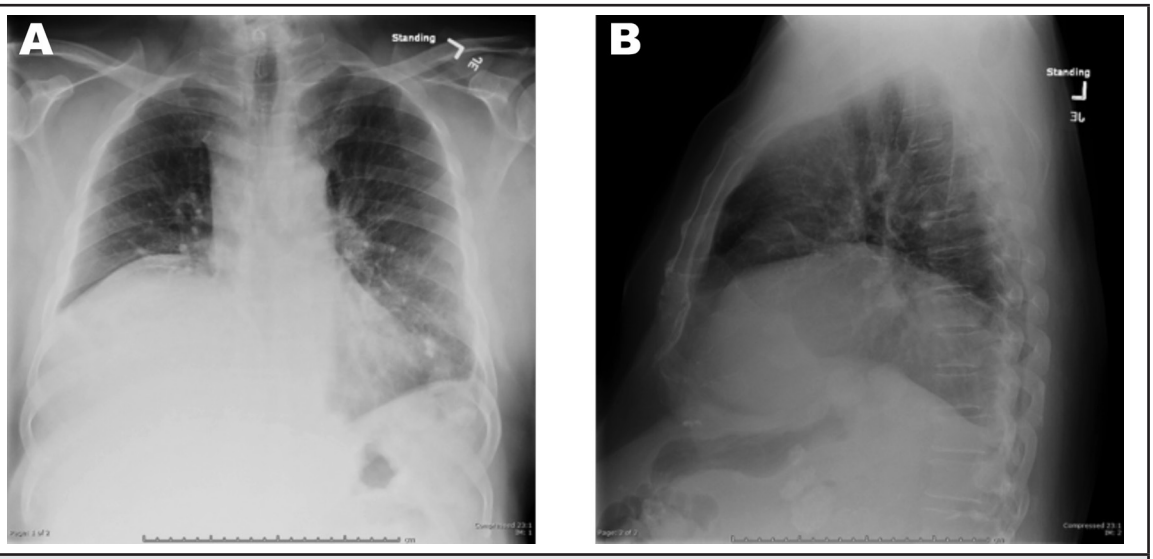

Figure 1. Plain anteroposterior (A) and lateral (B) radiographs of the chest demonstrating significant, abnormal elevation of the right hemidiaphragm.

and Right Upper Quadrant Ultrasound (RUQUS). Spirometry demonstrated a severely restrictive pattern with a Forced Vital Capacity (FVC) 1.89 liters (42% expected) and Forced Expiratory Volume in one-second (FEV_1) of 1.37 liters (41% expected) (ratio 0.72). Radiographs of the chest demonstrated abnormal elevation of the right lung base to the level of the right hilum and pulmonary arteries (Figure 1), and RUQUS revealed reaccumulation of a 19.2cm by 15.3cm hydatid cyst (Figure 2).

Ultrasound presence of calcifications, and absence of daughter cysts or active 'hydatid sand' classified the cyst as stage CE4 by WHO-IWGE classification system (Table 1). A repeat PAIR procedure was performed by interventional radiology with successful drainage of 3 liters of chalky, serosanguinous fluid. 98% dehydrated ethanol was injected into the cavity as a precaution for any remaining active protoscolices. Laboratory studies showed no eosinophilia, and echinococcal serologies

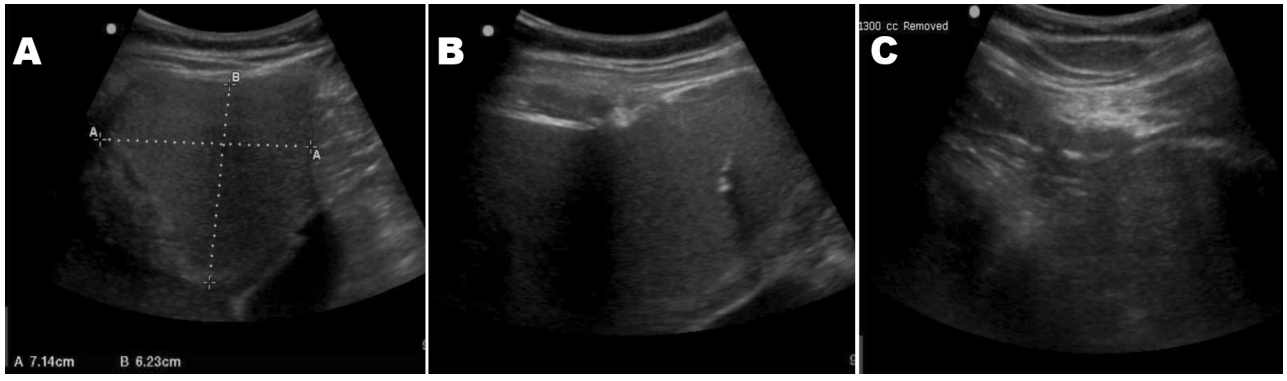

Figure 2. Ultrasound images during PAIR procedure. (A) Shows ultrasound image of cyst prior to procedure, with partial calcification and mixed hyper and hypo-echoic contents, consistent with an inactive, WHO-IWGE stage CE4 cyst. (B) Confirmation of drain placement in cyst. (C) Ultrasound of Liver after drainage of 1300cc of fluid.

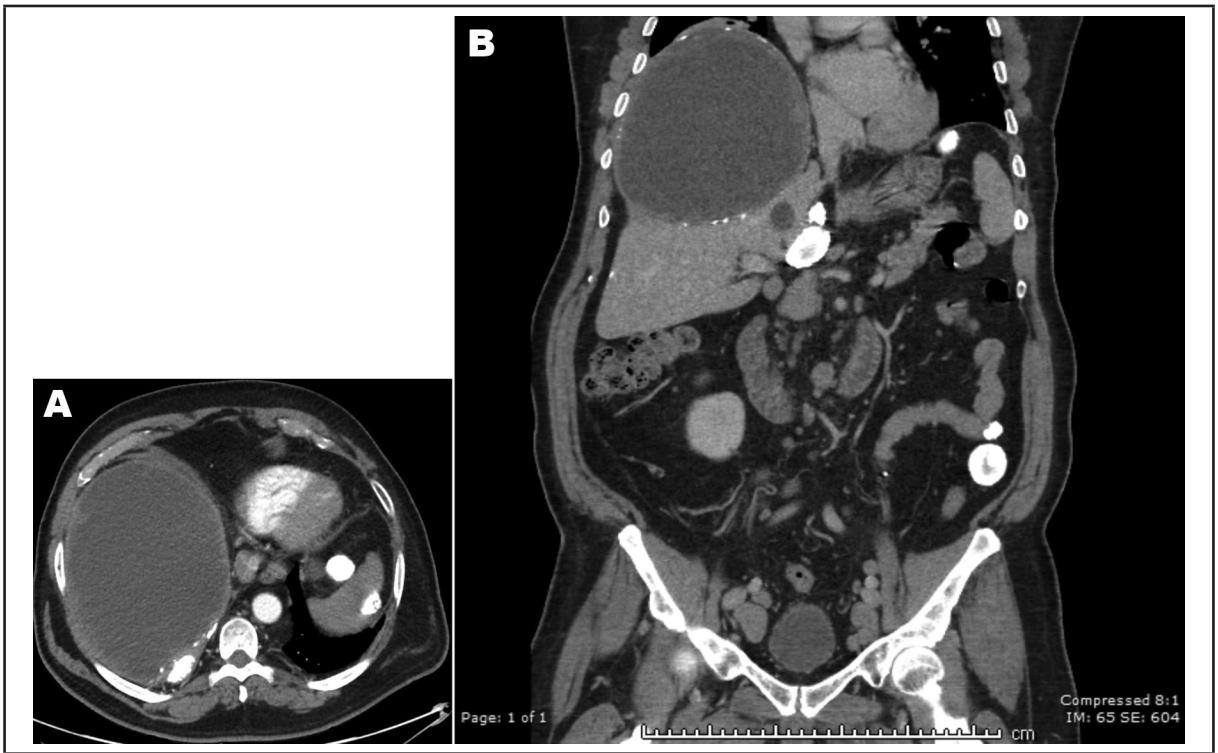

Figure 3. (A) Axial and (B) Coronal view on triphase liver CT demonstrates a nonenhancing, fluid attenuating hydatid cyst with scattered calcifications, measuring 15x19x14cm, with abnormal right hemidiaphragm elevation and compression of the right lung and right atrium.

were negative. Fluid analysis showed acellular debris and rare macrophages, but was negative for scolices, cysts, or hooklets, all findings consistent with inactive infection.

The patient experienced relief of his symptoms, however his activity-limiting shortness of breath returned four weeks later. 3-phase Computed Tomography (CT) of the liver and non-contrast Chest CT revealed re-accumulation of the cyst, persistent elevation of the right hemidiaphragm with compression of the right lung, and mass effect on the right atrium (Figure 3).

Due to the recurrence of the cyst following repeat PAIR procedure and the profound impact on his quality of life, the patient elected for surgical intervention. Total hepatic cystectomy was planned, however due to cyst adhesion to the right hemidiaphragm, partial cystectomy was performed by open hepatic wedge resection (Figure 4). To avoid potential protoscolex spillage 20% hypertonic saline was injected into the cyst before removal. Pathologic analysis showed fibrinous material, neutrophils, and lymphocytes, but again no scolices, cysts or hooklets. Surgical therapy resulted in lasting resolution of his dyspnea and right hemidiaphragm elevation (Figure 5).

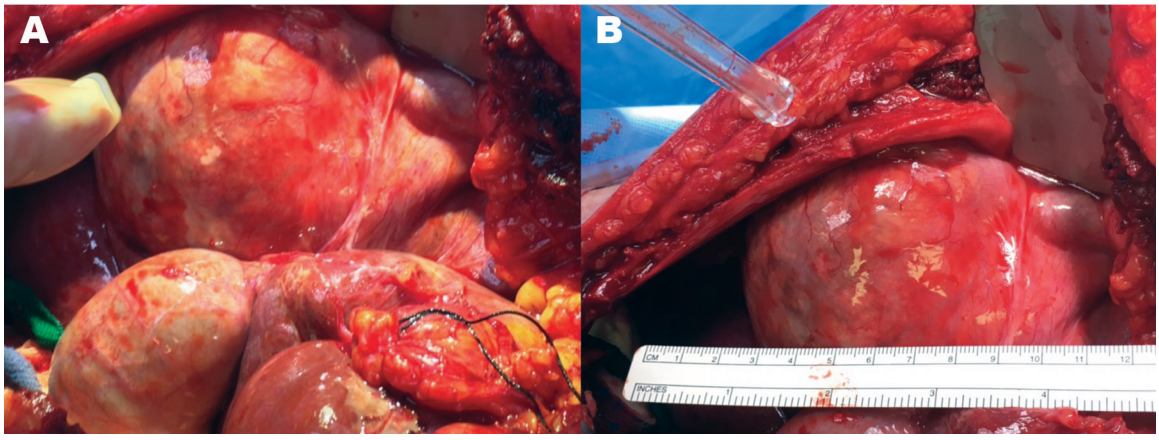

Figure . (A) and (B) Photographs taken intraoperatively shows the gross appearance of the hydatid cyst during open hepatic wedge resection.

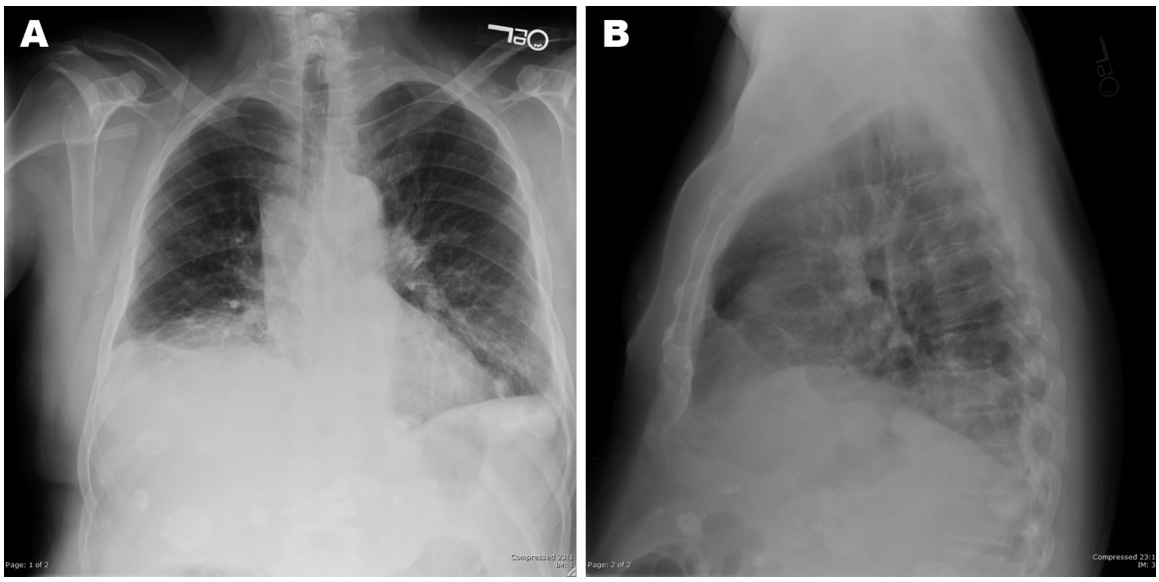

Figure 5: Plain anteroposterior (A) and lateral (B) radiographs of the chest taken postoperatively demonstrate marked improvement of right hemidiaphragm elevation.

Discussion

Hydatid cysts located within the abdomen are known to cause jaundice, abdominal pain, and nausea, but are not generally known to cause pulmonary dysfunction via mass effect.[2,3] It is especially unusual in industrialized nations to see an abdominal hydatid cyst of this size causing pulmonary symptoms, given the diagnosis of inactive disease by both ultrasound staging and negative serology. In AE, pulmonary pathology is manifested by cough, dyspnea, and pleuritic chest pain, but AE is not a common cause of restrictive physiology.[1,3] Usual complications of CE include cyst rupture with resultant risk for anaphylaxis and hydatosis within the peritoneum. However in this rare case, hepatic CE exerted mass effect on the right hemidiaphragm and lung, causing restrictive lung physiology.

Treatment strategies for human CE utilize a combination of observation, benzimidazoles, PAIR procedure, and, in certain cases, surgical cystectomy with caution not to rupture the cyst during surgery.[1,2,7,10,11] Surgical management is normally indicated for stage CE2 and CE3b cysts, with daughter vesicles, as well as when percutaneous treatment is unavailable. This patient's cyst was classified as WHO- IWGE stage CE4.[7,8] For cysts of stage 4 and 5, considered inactive, the preferred treatment is observation.[1,3] Due to recurrent growth causing restrictive lung physiology and symptomatic dyspnea from mass effect, surgical intervention was advocated for this patient.

It is unclear why the hydatid cyst recurred after 2 PAIR procedures in absence of high risk imaging features (CE1-CE3B). The accepted mechanism of recurrence is from spillage of protoscolices into the surgical field.[1,9] In inactive cysts, simple drainage, without injection of scolicidal agents, is considered sufficient treatment. In addition, it is uncommon to have recurrence after a PAIR procedure; in a study of 350 patients with hydatid disease of the liver treated with various methods, only 3.5% had recurrence in a 10-year follow up when treated with PAIR.[10] The outer layer of the cyst (pericyst) is a combination of endothelial cells, parenchymal cells, and dense fibrous tissue, around which a calcified layer forms (as seen in stage CE5 cysts). The surrounding liver collapses the cyst after drainage. This patient, with his longstanding disease, may have had an especially tough, thick cyst wall which resisted collapse, allowing reaccumulation of fluid. However, in one study with over 200 participants, only stage CE1 cysts required a repeat drainage.[12] The patient's medical history was negative for other etiologies that could cause extravascular edema such as heart failure, cirrhosis, or nephrotic syndrome. Despite official staging recommendations, the remote *Echinococcus* infection caused significant morbidity to this patient, requiring repeated percutaneous drainage procedures and finally surgery despite the inactive nature of his cyst and negative laboratory studies.[7,9,13]

The patient, although living in the United States, was an emigrant known to reside in Egypt, an endemic area, until adulthood. Human CE flourishes in temperate zones, notably the Mediterranean, central Asia and China, Australia, and within South America. While sheep and goats are the most common intermediate hosts, in North America, reindeer and moose also act as reservoirs.[2] Although both *E. granulosus* and *E. multilocularis* are endemic to certain parts of the country, such as Utah and Alaska, the majority of disease burden is borne by Asian, Pacific Islander, and Hispanic immigrants from endemic areas.[5]

This case highlights how a patient with risk factors and known history of CE should be investigated further for progression of disease when unexplained symptoms develop. In particular, repeat ultrasound of the liver and ELISA for cryptococcal antigen should be assessed to exclude active disease. Despite low risk findings, certain patients will benefit from intervention, especially those suffering from mass effect. In patients with a travel or emigration history consistent with possible exposure, it is important to keep a wide differential. This includes zoonoses and other unusual manifestations of parasitic diseases endemic to their country of origin. This case also highlights the importance of deviating from standard treatment practices when indicated by the patient's clinical presentation and quality of life.

Conflict of Interest

None of the authors identify any conflict of interest.

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